Appln No.: 09/674,975
Amendment Dated: October 29, 2003
Reply to Office Action of July 29, 2003

REMARKS/ARGUMENTS

This is in response to the Office Action mailed July 29, 2003 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Applicants note the Examiner decision on the restriction requirement. Applicants further point out, however, that claims 9 and 10 are generic with respect to the two identified Seq. ID numbers. Accordingly, should these claims be found to be allowable, it would be appropriate to recombine the other sequence ID, which is in essence a separate species from the elected Sequence ID, so as to avoid issuance of two separate patents directed to a genus and a species.

The specification has been amended to correct the typographical error noted by the Examiner. In addition, claim 12 has been amended to refer to breaking tolerance to CD20, rather than to a transmembrane protein generally.

A new declaration is provided in response to the Examiner's statement that the previous declaration is defective.

Applicants note that the Examiner has not returned the initialed Form-1449 for the Information Disclosure Statement filed February 12, 2002. An additional copy of this submission is enclosed, along with a copy of the returned postcard confirming receipt by the PTO. Consideration of the references is requested. It is also noted that the Office Action contained only one page of the 1449 from the Information Disclosure statement filed March 2, 2001. A copy of the second page is enclosed. Consideration of these references is requested as well.

The Examiner rejected the claims under examination under 35 USC § 112, first paragraph, for lack of enablement. The Examiner argues that the application is enabling for full length CD20 or the portion of CD20 given by Seq ID. No. 1. To the extent that the Examiner's rejection is understood, it seems that she is arguing that Seq. ID No. 1 is the only partial sequence specifically taught, and that the art is well aware that not all partial sequences will work. Because of this, the Examiner is apparently arguing that the claims must be limited to full length CD20 or the partial CD20 of Seq ID. No. 1. She further argues that coupling of the carrier protein is required. Applicants have amended the independent claims to refer to coupled carrier proteins only. As to the remainder of the rejection, however, Applicants respectfully disagree.

The Examiner's argument that the partial sequence of Seq. ID No. 1 is the only specific example of a partial sequence is plainly in error. Seq. ID No. 2 is also a specific example of a partial CD20 sequence. The fact that the Examiner has chosen to treat this as a separate invention does not in any way detract from the fact that this is part of the enabling disclosure for

the generic claims. Furthermore, while the Examiner has noted the CD20 partial sequences in Table 1, she has not offered any reasons why these do not provide additional scope of enablement. The Kd sequences start at amino acids 40 and 41 of the extracellular domain of human CD20 (Seq. ID No 3) while Seq ID No. 1 starts at amino acid 30. Thus, this information provides specific guidance as to the important portions of the sequence. Given the fact that the human extracellular domain (Seq. ID No. 3) is only 79 amino acids in length, this is substantial information sufficient to enable the claims. Thus, the assertions of limited disclosure are not well taken.

Finally, when considering enablement, it is important to look at the claimed invention as a whole. In the present case, Applicants invention is a vaccination method and vaccine composition that contains several components. It is not CD20-specific immunogenic sequences *per se*. Under the examiner's application of § 112, however, Applicants would be obligated to mention and test every conceivable sequence, and indeed to make additional inventions, in order to obtain full coverage for their invention. Applicants submit that this is not a correct application of the law.

As observed in *In re Fischer*,

> an inventor should be allowed to dominate the future patentable inventions of others where those inventions were based in some way on his teachings. Such improvements, while unobvious from his teachings, are still within his contribution, since the improvement was made possible by his work.

166 USPQ 18, 24 (CCPA 1970). In the present context, this means that not every example of CD20 sequences needs to be disclosed, else such domination would not be possible.

The Examiner has aptly demonstrated that other CD-20 specific sequences are known, for example via the Hooijberg reference, and are readily conceived. It is noted, however, that Hooijberg actually demonstrates the importance of the present invention in breaking tolerance, since it shows that mouse epitopes alone (as opposed to in the vaccine of the presentinvention) do not generate a T-cell response to CD20 in mice. In contrast, the mouse sequences tested in the present invention, which span several of the ineffective sequences of Hooijberg, was shown to be effective. Thus, the enablement question in this case iscorrectly stated as whether there is any reason to doubt the utility of a known CD-20 specific immunogenic sequence (whether already known or subsequently discovered) in the present invention as a vaccine. The Examiner has not offered any reasoning that would support such a conclusion. Accordingly, the enablement rejection should be withdrawn.

The Examiner has rejected the elected claims under 35 USC § 103 as obvious over the combination of Maloney et al, in view of Kwak et al., and US Patent No. 5,830,731. In making a rejection under 35 USC § 103, it must be remembered that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." Carella v. Starlight Archery and Pro Line Co., 804 F.2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1986) (citing ACS Hosp. Syss., Inc. v. Montefiore Hosp., 732 F.2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984)). "[T]he factual inquiry whether to combine references must be thorough and searching." McGinley v. Franklin Sports, Inc., 262 F.3d 1339, 1351-52, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001). This factual question cannot "be resolved on subjective belief and unknown authority," In re Lee, 277 F.3d 1338, 1343-44, 61 USPQ2d 1430, 1434 (Fed. Cir. 2002); "it must be based on objective evidence of record." Id. at 1343, 61 USPQ2d at 1434.

In the present case, the Examiner has cited Maloney for a teaching that CD20 is a suitable target for the treatment of B cell lymphoma. Maloney, however, presents a problem, because the passive immunization methodology employed requires creation of patient-specific antibodies. Quite evidently, Maloney recognized the need for better treatment regimen, but did not see an obvious alternative to meet this need.

Kwak describes the use of a patient-specific anti-idiotype vaccine directed against a surface immunoglobulin found on B cells. The vaccine contains an idiotypic determinant conjugated with an immungenic carrier protein such as KLH.

The '731 patent relates to cloning vectors and a cloning methodology for cell surface antigens. The patent provides a list of such antigens, that includes CD20. The patent also provides a generalized list of uses to which the various antigens can be put, which includes treatment of plasma neoplasms. There is no link in the '731 patent between any antigen, and any specific use to which that antigen may be put. Thus, the linkage that the Examiner is making, i.e, the selection of CDE20 antigen, and the selection of plasma neoplasms, and the specific subset of B cell lymphoma, is based entirely on the present application and not on the specific teaching of reference.

Based on the teachings of Maloney and Kwak, and the selective reading of the '731 patent, the Examiner asserts that the present invention would have been obvious. This assertion is made even though the present invention provides a non-patient-specific vaccine, while both Maloney and Kwak are patient-specific compositions.

It may be reasonably presumed that if persons skilled in the art thought that simply using CD20 with a carrier protein and an adjuvant as now claimed would have been successful, they would have done so, rather than exploring the much more difficult and costly avenues reflected

in Maloney and Kwak. Thus, the rejection is based a collection of isolated information selected using hindsight knowledge of Applicants invention, and does not present a *prima facie* case of obviousness. The U.S. Court of Appeals for the Federal Circuit has stated that "[t]he mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification." In re Fritch, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (citing In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984)). Although this statement is couched in terms of modifying the prior art, it is equally applicable to combining teachings found in the prior art. Specifically, the mere fact that teachings found in the prior art could be combined as proposed by an examiner does not make the combination obvious "absent some teaching, suggestion or incentive supporting the combination." Carella, 804 F.2d at 140, 231 USPQ at 647 (citing ACS Hosp. Syss., Inc., 732 F.2d at 1577, 221 USPQ at 933). Stated differently, "citing references which merely indicate the isolated elements ... are known is not a sufficient basis for concluding that the combination of elements would have been obvious." Ex Parte Hiyamizu, 10 USPQ 2d 1393, 1394 (POBAI 1988).

In this regard, it should be noted that the references cited by the Examiner in support of the enablement rejection lend credence to the general unpredictability of the art, and to the inadequacy of some epitopes of CD20 to induce an immune response, presumably as a result of tolerance. It is completely incongruous therefore that the Examiner should assert that an anti-idiotype reaction, an immune response to an entirely different type of antigen, should give rise to an expectation that active immunization to any antigen at all (and to CD20 in particular) will give rise to an immune response. Further, there is no reasonable reading of the '731 patent which would allow selection of the combination of the specific antigen (CD20) and the specific use (treatment of neoplasms) without reliance on the present specification.

For these reasons, Applicants submit that the rejection under 35 USC § 103 is in error and should be withdrawn.

This application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully Submitted,

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